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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,799	10/16/2003	David Reginald Adams	040283-0211	5143

22428 7590 10/21/2005

FOLEY AND LARDNER LLP  
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WASHINGTON, DC 20007

EXAMINER
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BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/685,799

Applicant(s)

ADAMS ET AL.

Examiner

Venkataraman Balasubramanian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 03 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☒ Certified copies of the priority documents have been received in Application No. 09/980,186.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/16/2003</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Applicant's election with traverse of Group VIII, claims 1-18, drawn to compound of formula I where  $X^1$ ,  $X^2$ ,  $X^3$  and  $X^4$  are CR along with the election of first species of claim 18, in paper filed on 10/3/2005, is acknowledged. Claims 1-18 will be examined to the extent they embrace the elected subject matter.

The traversal is on the ground(s) that there is common utility and substantial structural identity. This is not found persuasive for following reasons.

1. First of all both the above requirements are to be met with.

As stated in the previous office action, both these requirements are lacking as instant compound has more than one utility as evident from the instant specification and prior art cited in the Information Disclosure Statement. A prior art, which reads on instant elected utility obesity, would not be applicable treating stroke or schizophrenia and all other disease/disorders embraced instant claims unless applicants admit for the record that method of treating all these disease/disorders with the instant compound are equivalent.

Applicants rely on mode of action of the compound, namely its binding to HT2 receptor as a utility but if that is a utility then the diseases recited in the specification are additional utility for the instant compounds which by itself negate the common utility asserted by the applicants.

2. As stated in the previous office action the instant compound embraced by varying core groups constitute structurally dissimilar compounds. They are independent and distinct as the process of making and using them are different. They need

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not be used in combination. Furthermore, prior art, which reads on the instant elected or renders it an obvious variant, may not be applicable to non-elected heterofused ring systems.

Hence the instant claims fail to meet both the requirement stated above.

The requirement is still deemed proper and is therefore made FINAL.

### ***Claim Objections***

Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 which dependent on claim 1 recites a trifluoromethyl group as substituents on the aryl ring which outside the scope of claim 1. Note claim 1 is limited to alkyl and cannot include haloalkyl.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and shares the same indefiniteness.

1. Recitation of "and pharmaceutically acceptable salts and addition compounds thereof" in claim 1 renders claim 1 and its dependent claims indefinite as it is not

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clear whether the claim 1 is a compound claim or a composition claim with pharmaceutically acceptable salts and addition compounds. Note Markush choices should be in alternate form and in singular. Furthermore, it is not clear what is meant by addition compounds.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Jonas et al. US 3,853,878.

Jonas et al. teaches several heaxahydropyrazino[1,2-a]indole compounds, which include those claimed herein. See compound of formula II on col. 1, line 50 and note the definition of R. See col. 2 for compounds made, See example 2. Hence it is held that in order to make compounds shown in example 2, Jonas et al. had inherently made the intermediates, which are claimed herein. Note In re Petering et al 133 USPQ 275; In Re Schaumann, 195 USPQ 5.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mokrosz et al., Med. Chem. Res. 3: 240-248, 1993 for reasons of record. To repeat:

Mokrosz et al. teaches rigid arylpiperazines as CNS agents, which include a compound with ethyl group on the piperazine ring. See compound 7 on page 241, and process of making on page 247.

While said compound doesn't anticipate the scope of instant claims in view of the proviso in claim 1, they are very closely related, having a methyl group on the phenyl ring vs. unsubstituted phenyl ring compound of the reference. However, compounds that differ only in having H vs Me are not deemed patentably distinct absent evidence of superior or unexpected properties. See for compounds that differ only as H vs Me in the phenyl ring, In re Wood 199 USPQ 137; In re Lohr 137 USPQ 548. Additionally, applicants should note that the prior art N-ethyl piperazine as shown by Mokrosz et al. is active at the 5HT receptor and hence one would be motivated to make and evaluate the compound with a methyl group in the phenyl ring.

Thus it would have been obvious to one skilled in the art at the time of the invention was made to expect instant compounds to possess the utility taught by the applied art in view of the close structural similarity outlined above.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bos CA 2,097,465 in view of Mokrosz et al., Med. Chem. Res. 3: 240-248, 1993.

Bos teaches several tetrahydropyrazinoindole compounds, composition and method of use treating several central nervous disorders including obesity. See compound of formula I on page 1 and note the definition of R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> groups and the diseases for which these compounds are useful. See pages 2-13 for details of the preferred embodiments, schemes for making and pages 13-16 for testing. See examples 1-14 on page 16-37 and example A, B for composition.

Instant claims differ from Bos in requiring pharmaceutical composition containing compound of formula I, which are hexahydropyrazinoindole

The secondary reference, Mokrosz et al., as noted in the above 103 rejection, teaches hexahydropyrazino[1,2-a]indole and N-ethyl- hexahydropyrazino[1,2-a]indole as bioactive compounds useful for 5HT receptor. On page 241, Mokrosz et al. teaches reduction of tetrahydropyrazinoindole to hexahydropyrazinoindole. Mokrosz et al. also demonstrates that both tetrahydropyrazinoindole and hexahydropyrazinoindole are active in the 5HT assay. See page 243, Table 2. Thus there is a clear-cut teaching of equivalency of both tetrahydropyrazinoindole to hexahydropyrazinoindole in their activity toward 5HT.

Thus one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and make compounds variously substituted in heaxahydropyrazino[1,2-a]indole based on the reduction of tetrahydropyrazino[1,2-a]indole as permitted by the combined references and expect resulting compounds (instant compounds) and its pharmaceutical composition to possess the uses taught by the art in view of the equivalency teaching outline above.

### **Conclusion**

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Acting Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson whose telephone number is (571) 272-0661.

The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you



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have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

*Venkataraman Balasubramanian*  
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10/14/2005